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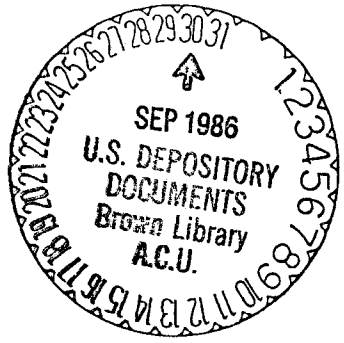


# METHAQUALONE

The recent rise in street abuse of methaqualone, a non-barbiturate sedative originally believed to be non-addictive, has presented serious problems of overdose and addiction in various sections of the United States. It began on college campuses in the Midwest and has since spread to high school and college campuses on the East and West Coasts.

Methaqualone was introduced by M.L. Gujral in India in 1950, and it has been used clinically for the past 10 years, mostly in Europe, as a sleeping aid and a daytime sedative. In the United States, methaqualone is marketed under various brand names: Quaalude (Rorer), Sopor (Arnar-Stone); or its hydrochloride, Parest (Parke-Davis), Optimil (Wallace) and Somnafac (Smith, Miller and Patch). In England, methaqualone is prescribed in the hydrochloride form as Melsedin (Boots), or in combination with the antihistamine, diphenhydramine, as Mandrax (Benadryl). Some of the street names for the drug and its abuse are derived from the brand names, i.e., Quaalude, "luding," Sopors, "soapers."

Methaqualone gained popularity on the street because it was alleged to be a safe and non-addictive sedative. As street abuse, overdoses, and addiction were reported, the abuse potential and harmful effects of methaqualone have been recognized by medical and scientific societies, and have led to attempts to get the drug reclassified and placed under the Controlled Substance Act of 1970. At the present time, the Drug Enforcement Administration is considering the reclassification of methaqualone which could result in a change in the drug's legal status.

## Patterns of Use

There are many factors involved in the widespread illicit use of the drug among young people. One important factor was the belief among physicians and laymen alike that the drug was a sedative hypnotic with many of the properties of barbiturates but without the potential for addiction, and because of its alleged safety an effectiveness, it was prescribed quite freely for the relief of insomnia. Thus, as a legal drug that was quite available on prescription, methaqualone became the subject of extensive abuse.

Another reason the drug culture "discovered" and abused methaqualone was that strong enforcement efforts, by the then U.S. Bureau of Narcotics and Dangerous Drugs (now part of DEA), against many of the illicit drugs of abuse and the legal drugs with abuse potential resulted in a significant decrease in the availability of amphetamines, cocaine, heroin and marihuana on the street.

Abusers usually obtain the drug from legal pharmacies by means of forged prescriptions. The drug is also available through the black market where it has been diffused from its legal channels of distribution. In areas where there is a concentration of pharmaceutical houses manufacturing the drug, the black market is saturated with methaqualone at comparatively low prices.

The drug itself has effects which make it conducive to abuse. The trend has changed seemingly from drugs that accelerate motives of aggressiveness, mysticism and anxiety to this one which induces quiescence. A methaqualone culture appears to have developed where Sopor parties are frequent. In New York City, clubs called "juice bars" are appearing which cater to users of the drug, and appropriately serve juice to take with the pills, rather than alcoholic beverages, which can intensify the drug's effects and increase the chances of overdose.

Methaqualone has been acclaimed as an aphrodisiac or love drug because users tend to feel more relaxed, friendly, receptive and uninhibited. The notion that it enhances sexual performance and improves sexual pleasures, one of its most attractive selling points, is actually unfounded in reality. While the

drug lowers inhibitions, and increases sexual desires, it actually lowers the ability to perform sexually. When larger doses of methaqualone are ingested, especially in combination with alcohol, it is more likely that the user will enter into a stupor, which tends to make sex almost impossible.

Abuse of methaqualone has been reported in the United States, England and Japan. Mitcheson et al. (1971) and de Alarcon (1969) report its abuse by heroin addicts to help them sleep or to give them a "kick." Mitcheson states, however, that because methaqualone does not dissolve in water, the heroin addicts he interviewed were more inclined to use barbiturates they could inject rather than to take methaqualone orally.

Street users take methaqualone, as they do other illegal drugs, to get high. Ager (1972) describes "luding out" as taking 300 to 450 milligrams (mg.) of methaqualone with wine.

> The combination directly produces a pleasant sense of well-being, an increased pain threshold, an impairment in proprioceptive sense, which induces severe ataxia, and a pins-and-needles paresthesia of the fingers, lips, and tongue. Rather than alarm the user, the painless pleasant ataxia frequently gives him feelings of indestructibility, which, in turn, lead to euphoria. I have received several reports of users in this ataxic euphoria state falling down flights of stairs, not feeling the bruises until the following day.

Street use and abuse have also been noted by Schnoll et al. (1972), Matthew (1971) and by Bridge and Ellinwood (1973). The users describe the sensation produced by methaqualone as "peaceful," "calm," "a rush," or "drunk."

> Methaqualone has become a particularly popular drug among college students who take the drug (300-600 mg.) and then fight off the urge to sleep. This they claim gives a high. Others use it just for the sedative effect. It is sometimes taken with alcohol, a practice called "luding out" after the trade name Quaalude. Other street names for the drug are "mandrakes" after the British drug Mandrax ... and "soapers" after the trade name Sopor.

Methaqualone is not manufactured underground as are most of the other drugs of abuse. The pills on the street are pure, legally manufactured pills, which are obtained from pharmacists with legally or illegally obtained prescriptions. Problems with medical complications arising from impurities and additives usually found in street-manufactured drugs are not encountered with methaqualone.

## Chemistry and Pharmacology

Methaqualone (2-methyl-3-o-tolyl-4(3H)-quinazolinone) is a 2,3-disubstituted quinazolone. It is one of the most potent of the quinazolone series of hypnotic compounds. Methaqualone is orally active, soluble in alcohol and ether, and only slightly soluble in water.

Following its ingestion, methaqualone is readily absorbed from the gastrointestinal tract. It is transported in the blood plasma, apparently following an enterohepatic route, and is distributed in body fat, the liver and brain tissue. The liver is the primary site of metabolism and the drug is excreted and biotransformed through the bile and kidneys. Methaqualone produces an appreciable increase in the activity of the liver microsomal enzymes, more so than noted with barbiturates.

Animal studies reveal that methaqualone depresses polysynaptic reflexes in the spinal cord in high doses but has little effect on either monosynaptic reflexes, spinal ganglia, the myoneural junction, or skeletal muscle. Methaqualone raises the threshold for electrically induced seizures, indicating that the drug acts centrally in the brain, depressing the pathways in the thalamocortical portion. Unlike the barbiturates, methaqualone's action is not due to a direct depression on the midbrain reticular system, nor does it cause depression of the medulla.

Methaqualone is not prescribed for women who are pregnant. Animal experiments have indicated some teratogenic activity. Investigations in animals have also demonstrated that the toxic dose of the drug to the fetus is the same as that given to the mother, indicating that methaqualone does pass the placental barrier.

The standard hypnotic dose of methaqualone to induce sleep is 150 to 300 mg. Seventy-five mg. is the daytime sedation dose. Coma has been known to occur following 2.4 grams (gm.) of Quaalude. Eight to 20 gm. have produced severe toxicity and death. Overdoses of methaqualone are less often marked by cardiac and respiratory depression than overdoses of oral barbiturates. But like barbiturates, methaqualone has an additive effect when used with most depressants, including barbiturates, antianxiety and antipsychotic agents, and alcohol. Methaqualone can produce a comatose state without interfering much with pain response, pulse or respiration. Overdose can result in delirium, restlessness, hypertonia, and muscle spasms leading to convulsions.

## Addiction Potential

Some reports of tolerance (increasing resistance to the pharmacologic effects of a drug) to methaqualone have appeared in the literature. One study, conducted by Brown et al. (1969), reported cases where plasma levels of methaqualone ranged from 0.2 to 8.3 milligrams per milliliter (mg./ml.). Very few of these patients

demonstrated features of poisoning, although levels exceeding 3.0 mg./100 ml. were regarded as dangerous a few years earlier. The conclusion of the investigators was that tolerance had developed.

Physical dependence on methaqualone was reported by Madden (1966). He discussed four cases of dependency on Melsedin and pointed out:

> Between them these cases demonstrate at least three of the four features designated by the W.H.O. (World Health Organization) Committee as characteristic of drug dependency of the barbiturate type. The features definitely shown are a strong desire to continue taking the drug, a tendency to increase the dose (partly due to development of tolerance), and psychic dependence on the effects of the drug.

Madden's report was challenged because he observed no withdrawal syndrome, the fourth feature of barbiturate-like dependency. Schnoll et al. (1972) describe three cases where a withdrawal syndrome was indicated. The subjects were taking from 600 mg. to 3,000 mg. of methaqualone daily. When the drug was withdrawn, insomnia, abdominal cramps, headaches, anorexia and nightmares were experienced. One subject had been abusing barbiturates before she began using methaqualone. She experienced no withdrawal symptoms when she switched, which suggested a cross tolerance between barbiturates and methaqualone. Ewart and Priest (1967) found delirium tremens, characteristic of barbiturate withdrawal, to be a main effect of withdrawal from methaqualone. It has been acknowleged that withdrawal from sedative-hypnotics is more severe than withdrawal from an opiate drug. Some users report that becoming addicted to methaqualone is easier than becoming addicted to opiates.

## Physiological Effects

As a sedative hypnotic, the primary physiological effects of methaqualone are induction of sleep and sedation. Normal sleep consists of two alternating states. The electroencephalogram (EEG) of orthodox sleep is characterized by slow waves and spindles. The paradox or rapid eye movement (REM) sleep (the time when dreaming occurs) is characterized by a low-voltage EEG devoid of sleep spindles. An effective hypnotic should duplicate normal sleep as closely as possible, although most do not completely. Almost all soporific doses of central nervous system (CNS) drugs depress REM sleep to some extent. The increase of REM sleep after withdrawal of a CNS depressant drug is called REM rebound.

In sleep studies by Davidson et al. (1970) and Goldstein (1970), Mandrax and methaqualone did not significantly alter REM sleep. Soulairac and Gottesmann (1967) found that in male rats methaqualone induced sleep of entirely normal appearance, with occasional spindles observed in the EEG more often than in the

controls. Kales et al. (1970) did find that 300 mg. of methaqualone suppressed REM sleep in humans, and when withdrawn caused REM rebound; 150 mg. did not. Evans and Ogunremi (1970) found an erratic effect of Mandrax on REM sleep, but found no REM rebound on withdrawal.

In a study using rats, Baylor and Himwich (1961) found that low intravenous doses of methaqualone produced electrocorticogram (ECG) synchronization, a shift away from wakefulness towards sleep. In high doses, it abolished the arousal response to auditory and pain stimuli.

Norris and Telfer (1969) found no significant changes in heart rate, respiration or blood pressure when administering 250 mg. of methaqualone as a pre-anesthetic medication. Saxena et al. (1972) found no marked changes in the vital signs when injections of 5 milligrams per kilogram (mg./kg.) to 20 mg./kg. of methaqualone were administered to patients before short surgical procedures. He did observe muscle spasms following the onset of sleep, lasting for approximately 1 minute.

Swift et al. (1960) found that doses of 75 mg./kg. caused mice and rats to completely lose their righting reflex. Doses of 120 mg./kg. in dogs caused muscle incoordination and a mild pre-anesthetic type excitement. This was followed by vomiting, urination and defecation in every dog tested. Three hours after administration of the drug, the dogs were immobilized by a generalized flaccid paralysis. The paralysis lasted for more than 8 hours, and the animals did not fully recover for 48 hours after the drug's administration. In all animals tested, Swift found that methaqualone had no effect on the heart rate and did not produce abnormal pupil dilation.

Adverse physiological effects to methaqualone in humans include headache, hangover, menstrual disturbance, tongue changes, dryness of the mouth, cracking at the angles of the mouth, nosebleeds, depersonalization, dizziness, skin eruptions, numbness, pain in the extremities, diarrhea, and anorexia.

## Therapeutic Use

Controlled clinical studies have shown methaqualone alone or in combination with dephenhydramine hydrochloride to be an effective sedative hypnotic. Its onset of action, duration of action, and effectiveness in comparison to other sedative hypnotics or barbiturates have been demonstrated in studies by Haider (1968), Parsons and Thompson (1961), Adamson (1970), and Derbez and Grauer (1967). Haider and Derbez found it to be especially effective with geriatric patients. In a double-blind triple crossover investigation by Meares et al. (1972), little difference was found between the hypnotic effects of Mandrax and Mogadon, another non-barbiturate sedative hypnotic. More incidents of morning hangover were found with Mandrax than with Mogadon. Curiously, about 20 percent of this sample thought the quality of sleep after taking the placebo to be better than that after taking either of the drugs.

Although not an analgesic itself, methaqualone potentiates the analgesic action of codeine. Used as a pre-anesthetic medication, Norris and Telfer (1969) found Mandrax to work better than methaqualone alone. There was little change in vital signs; postoperative nausea and vomiting were rare. Saxena et al. (1972) also found methaqualone to exhibit no change in vital signs after intravenous injection as a sole anesthetic in short surgical procedures. They also used methaqualone as a backup anesthetic for nitrous oxide with apparent success.

## Treatment of Overdose

Management of a methaqualone overdose varies somewhat from a barbiturate overdose. Supportive therapy should be given to maintain vital functions. In cases of mild overdose, the victim should be kept under close supervision to sleep off the effects of the drug. Diuresis is not recommended since pulmonary edema and myocardial damage can occur. If the drug was recently ingested and the victim is still conscious, elimination of the gastric contents is advised. Although Lawson and Brown (1967) performed gastric aspiration and lavage when cough and gag reflexes were present, caution should be used since methaqualone, unlike barbiturates, produces coma without affecting the gag reflex.

## Legal Aspects

Methaqualone is classified as a legend drug, and is available by prescription only. There are no Federal laws governing the unauthorized possession, manufacture or distribution of a legend drug, and thus penalties vary from state to state. Current investigation by the Drug Enforcement Administration and the Food and Drug Administration has resulted in the Drug Enforcement Administration considering the addition of methaqualone to Schedule II of the Controlled Substance Act of 1970. The requirements for a drug being placed under Schedule II are: the drug or substance has a high potential for abuse; has a currently accepted medical use in treatment in the United States, or a currently accepted medical use with severe restrictions; and abuse of the drug or substance may lead to severe psychological or physical dependence.

## Issues and Opinions

Although methaqualone has been clinically demonstrated as an effective hypnotic, controversy abounds as to its abuse and addiction potential.

I wish to report that abuse of methaqualone within the United States has taken on qualities of a silent epidemic, with large and ever increasing numbers of college students, on campuses in areas as distant as Ohio, Eastern Pennsylvania, and Florida, privately taking the drug for entertainment, even to the exclusion of marihuana.

--Steven A. Ager (1972)

Nationally, quaalude is running an even race for popularity with illicit methadone. Most people who get quaalude by legal prescription take it for fun rather than for sleep. If you eat a lot you build up a tolerance. With heroin and other opiates both the amount of the drug needed to get you stoned and the amount needed to kill you go up proportionally. With quaalude the fatal dosage remains about the same even though you need more and more to get off. Eventually the fatal dosage and daily dosage become dangerously close--close enough so that a couple of good drinks could tip it over into a coma.

--John Steinbeck (1972)

Mandrax ....poisoning is a common problem. In the first six months of 1966 over-dosage with Mandrax accounted for 5 percent of admissions to the Poisoning Treatment Centre at Edinburgh Royal Infirmary. In the last six months of 1967 this proportion has risen to 10 percent, so that Mandrax now ranks with barbiturates and salicylates as the drug most often taken in self-poisoning.

--Henry Matthew et al. (1972)

In recent months I have been asked to see a number of cases of anxiety and depression who in the initial stages of their illness have been prescribed methqualone for insomnia. I often found it difficult to switch them over to less powerful hypnotics even after the main psychiatric illness had been treated.

--R. de Alarcon (1969)

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